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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,545	09/03/1999	COLIN R. DUNSTAN	A-605	5554

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EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 10/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/389,545

Applicant(s)

DUNSTAN, COLIN R.

Examiner

Larry R. Helms

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-- The MAILING DATE of this c mmunication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 August 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-58 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-58 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- ☐ Interview Summary (PTO-413) Paper No(s). _____
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____

DETAILED ACTION

1. Claims 41-58 are pending and under examination.
2. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

Rejections Withdrawn

3. The rejection of claims 48-52 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in view of arguments and showing that fusion proteins are used in a method of treating abnormal bone formation (see response at page 3).

Response to Arguments

4. The rejection of claims 41-46, 48-49, 53-58 under 35 U.S.C. 112, first paragraph is maintained.

The response filed 8/11/03 has been carefully considered but is deemed not to be persuasive. The response states that the Examiner's characterization of Table 1 of WO 97/23614 is incorrect and Table 1 shows that the following OPG polypeptides have biological activity: murine OPG 22-401-Fc, 22-194-Fc, 22-185-Fc, 22-401, 22-401(C195), 22-401(C202), 22-401(C319), 22-401(C400), 22-194, 22-200, 22-203, 22-235; and human 22-401-Fc, 22-201-Fc, 22-401-Fc(P26A0), 22-401-Fc(Y28F), 22-401,

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27-401-Fc, 29-401-Fc, 32-401-Fc and 22-194-Fc in example 12 and in the instant application 22-194 and 22-201 fused to Fc (see page 2 of response) and based on the teachings of WO 97/23614 and the instant specification one skilled in the art would recognize that other OPG molecules could be tested for activity.

In response to this argument, while Table 1 does show more examples of 22-401 with a cysteine residue substituted at a specific position only residues 22-401 is active. In addition the only human molecules is 22-401 fused to Fc or 22-401 without Fc fusion. In addition the two molecules of 22-194 and 22-201 are fused to Fc not unfused as encompassed by the claims.

The specification is enabled for OPG polypeptides that are unfused and consist of residues 22-401 of unfused human OPG and only unfused OPG of residues 22-194, 22-200, 22-201, 22-293, and 22-355 of mouse. Table 1 of WO 97/23614 teaches only these constructs result in bioactivity. In addition the art of Simonet et al (Cell 89:309-319, 1997 teaches that loss of the C-terminal portion up to amino acid 194 did not affect activity (see page 315). Therefore the prior art teaches only specific OPG molecules are active and the claims still encompass any OPG of any residues as well as any truncated polypeptides of OPG. In addition, claim 48-49 encompasses OPG fused to any polypeptide and the specification only enables a Fc Δ C-OPG(22-194) fusion protein for treating bone loss.

5. The rejection of claim 43 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The response filed 8/11/03 has been carefully considered but is deemed not to be persuasive. The response states that the specification on page 8, lines 7-10 states "...wherein full length mature OPG has 380 amino acids, such as from residues 22-401 inclusive..." (see page 3 of response). Does the "mature" form only have 380 amino acids and any sequence of 380 amino acids? Thus, it is still unclear what mature means because in addition the definition recites "such as from 22-401" is this the mature form of is other forms contemplated?

6. The rejection of Claims 41-58 under 35 USC 103(a) as being unpatentable over Boyle et al (WO 97/23614) and further in view of Conte et al (Annals of Oncology 5:S41-S44, 1994) and Simonet et al (Cell 89, 309-319, 1997) is maintained.

The response filed 8/11/03 has been carefully considered but is deemed not to be persuasive. The response states that the rejection is clearly based on hindsight with knowledge of the invention and the examiner is picking and choosing various parts of Boyle, Conte, and Simonet to arrive at the claimed invention and it is clear that Conte contemplated further trials with other bisphosphonates in combination with chemotherapy but did not in any way suggest that an anti-resorptive agent should be combined with chemotherapy to treat bone loss. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight

reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In addition, Conte et al reference predates the Simonet reference and one skill in the art reading Simonet, which uses OPG for treatment of pagents disease and osteolytic metastasis, would conclude that OPG is just as effective as pamidronate and would combine the benefits of OPG with chemotherapy because OPG is similar in effect to pamidronate as taught by Simonet. There is no need to substitute pamidronate for OPG as suggested in the response because the art recognized OPG for treatment of bone loss associated with cancer and chemotherapy in combination with bone loss prevention molecules. In addition, because the claims recite open language the claims encompass a method that uses OPG, pamidronate and chemotherapy in combination.

7. The rejection of claims 42-47, 56-58 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is maintained.

The response filed 8/11/03 has been carefully considured but is deemed not to be persuasive. The response states that at page 30, lines 32-36 it is stated that "[t]he fusion polypeptides of the invention are used in the ...prevention and/or treatment of

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replacement of structurally sound bone with structurally abnormal bone." and also at page 31, lines 25-29 which is a reference to Paget's disease (see page 3 of response). In response to this argument, the specification supports fusion polypeptides of OPG not just any OPG polypeptide or truncated polypeptide as recited in the claim.

Applicant is required to provide specific support for the limitation in the specification as originally filed or remove it from the claim.

Conclusion

8. No claim is allowed
9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

11. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,
Larry R. Helms Ph.D.
703-306-5879



LARRY R. HELMS, PH.D
PRIMARY EXAMINER